REMARKS

Claims 1-45 are currently pending in this application. Claims 1-45 will remain pending on entry of the current amendments. Claims 1-40 and 42-45 stand withdrawn.

Interview Summary

On January 31, 2003, Applicant's representative conducted a telephonic interview with the Examiner of record at which time Applicant affirmed election, to the extent Applicant was required for prosecution of the subject application, of the species of claim 41 associated with determining whether a sample of an individual's body fluid contain antibodies specific for the gene product of the ATP-dependent iron transporter ABC-7 gene.

Election of Species Requirement

Claim 41 is directed to a method of screening for cancer by determining the presence of antibodies specific for one or more of the proteins selected from the Markush group of HOXA7, HOXB7, ABC-7, Arf-1 and the protein encoded by a EcoRI/XhoI fragment of bacteriophage λ clone 44B.1. Thus, claim 41 is a generic claim, and Applicant has elected a species (ABC-7) within the genus defined by the Markush group. Applicant notes that the Examiner's acknowledgement of Applicant's election of species without traverse confirms Applicant's interpretation of the disposition of the restriction requirements in the subject application: namely that claim 41 is a genus claim to which Applicant was required to elect a species.

Amendments

The specification and claims 1, 2, 5, 9, 10, 12, 15, 17, 18, 30, 41, 42, 43 and 45 have been amended herein to recite ATCC Deposit Accession No. PTA-3170. The specification has further been amended to address the Examiner's concerns regarding the proper presentation of trademarks recited throughout the specification. Additionally, the specification has been amended to delete the text providing an embedded hyperlink, in accordance with the provisions of MPEP § 608.01(p). Accordingly, Applicants assert that no new matter is introduced into the specification by way of the present specification and claim amendments.

Objections

Claim 41 was objected to because the "claim is alternatively drawn to the subject matter of non-elected inventions." *See* Paper 15, page 4, lines 10-11. Applicant respectfully asserts that further amendment of claim 41 is unnecessary, in light of the species election dated December 18, 2002 in the subject application. Generic claim 41 is directed to a method of screening for cancer by detecting the presence of antibodies specific for one or more members of the Markush group consisting of five (5) individual proteins, the presence of antibodies to one or more of any of these proteins indicative of an increased likelihood of cancer. Applicant has complied with the Examiner's requirement to elect a species for examination, said species encompassed by *generic* claim 41. Further amendment to claim 41 is unnecessary, as Applicant has fully complied with the Examiner's requirements and 37 C.F.R. § 1.146.

Rejections

Rejections under 35 U.S.C.§ 112, 1st paragraph

Claim 41 was rejected under 35 U.S.C. § 112, 1st paragraph as allegedly "containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention." *See* Paper 15, page 4, lines 19-22. More specifically, the rejection purports that the "teachings of the specification are insufficient to enable the skilled artisan to use the claimed invention with a reasonable expectation of success without having the need to perform additional and an undue amount of experimentation." *See* Paper 15, page 4, lines 23-25.

The rejection further states that "[t]he specification does not exemplify the use of the claimed invention," but instead teaches that autologous anti-tumor antibodies require further analysis and assessment. Allegedly, the specification lacks a disclosure of factual evidence "to support the assertion that the claimed invention can be used to ascertain the likelihood that an individual has cancer." *See* Paper 15, page 5, lines 16-17.

Applicant respectfully disagrees and traverses this rejection.

As an initial matter, Applicant asserts that the claimed invention adequately satisfies the utility requirements under the Patent Laws. Even though the claimed invention was not formally rejected under 35 U.S.C. § 101, the rejection raises issues of utility that Applicant will presently

address. The rejection cites Gadducci *et al* for the proposition that, as a corollary of Gadducci's findings that anti-p53 antibodies lack prognostic value, that "the skilled artisan could not predict the utility of Applicant's disclosed discovery without having the need to perform additional and an undue amount of experimentation to assess the clinical significance of the discovery of a patient having antibodies that bind ABC-7." *See* Paper 15, page 6, lines 6-9. The rejection further cites as support Creaney *et al* (Br. J. Cancer, 84:52-56 (2001)) and Mack *et al* (Oncol. Rep., 7:669-74 (2000)) for the findings that anti-p53 antibodies do not serve as either a prognostic or diagnostic indicator in malignant mesothelioma, and that there is no statistical correlation between the presence of anti-p53 antibodies and a diagnosis of small cell lung cancer, respectively.

Applicants respectfully point out that the disclosures of Creaney *et al* and Mack *et al* deal with malignant mesothelioma and small cell lung cancer, respectively, while the presently claimed diagnostic methods are directed to the detection of ovarian cancer. Therefore, any conclusions drawn from these two references are applicable to malignant mesothelioma and small cell lung cancer, not ovarian cancer.

The Gadducci *et al* reference was quoted as having found "that the presence of antibodies against p53 in the serum of patients having ovarian cancer had no prognostic relevance." *See* Paper No. 15, page 6, lines 2-3. Applicants respectfully point out that the Gadducci *et al* reference evaluates the relevance of serum anti-p53 antibodies in a prognostic setting, while Applicant's claimed method relies on autoantibodies against one or more of the recited proteins in a diagnostic setting. Thus, Gadducci *et al* deals with the evaluation of anti-p53 antibodies to foretell the probable course of the disease or to forecast the outcome of the disease which is already known to exist, while the claimed method relies on autoantibodies to determine the presence of a disease. That Gadducci *et al* failed to find anti-p53 antibodies useful as a prognostic indicator of disease progression does not jeopardize the use of autoantibodies of the claimed method as a diagnostic tool.

In light of the Tockman *et al* reference (cited in the office action), the rejection further holds that a showing that the claimed method is validated against acknowledged disease end points and contains predictive value confirmed in prospective population trials is necessary "prior to successful application of newly described markers.". *See* Paper No. 15, page 6, lines 27-30. Applicant respectfully disagrees that a showing of this magnitude is necessary to satisfy

the utility requirements. The burden that must be met to satisfy the utility requirement of 35 U.S.C. § 101 is not great. The Federal Circuit has supported this rationale by stating that "[t]he threshold of utility is not high: An invention is 'useful' under section 101 if it is capable of providing some identifiable benefit." Juicy Whip v. Orange Bang, 185 F.3d 1364, 1366 (Fed. Cir. 1999) (quoting Brenner v. Manson, 383 U.S. 519, 534 (1966); *emphasis added*).

In order to satisfy the requirements of 35 U.S.C. § 101, Applicant must provide a utility that is specific (to the subject matter claimed) and substantial (e.g., a real world use), as well as credible. *See* M.P.E.P. § 2107. Applicant has provided at least one specific and substantial utility that is also credible. The specification discloses autologous antibodies to five specific intracellular antigens in the serum of patients with ovarian cancer, including an autologous antibody specific to ABC-7 (ATP-binding iron transporter). The specification further states that

> [b]ased on the observation of autologous antibodies to these antigens in association with cancer, the present invention provides a screening method for use in identifying individuals which are likely to have cancer. A positive result to this screening assay will help support a diagnosis of cancer *or at the very least justify additional diagnostic activity to confirm the likelihood suggested by the positive screening assay.*

See specification, page 22, line 26 extending to page 23, line 3 (*emphasis added*). Substantial value is provided by assays that (1) conclusively prove the presence of a disease state or (2) provide findings sufficient to justify additional confirmatory testing. Applicant submits that extensive population trials are unnecessary to validate the utility of a procedure that already has specific, substantial and credible utility on its face to one of skill in the art. Based on the findings presented in the specification, the utility of Applicant's claimed invention is specific, substantial and credible. Accordingly, Applicant asserts that the claimed invention satisfies the utility requirements under 35 U.S.C. § 101.

Regarding the enablement aspects of the rejection, Applicant asserts that the claimed invention does not require undue experimentation in order to provide one skilled in the art with the expectation of successfully practicing the claimed invention. Applicant has provided ample teachings to those of skill in the art to make and use the claimed invention without undue experimentation. That some experimentation is necessary to achieve the claimed invention is not determinative of the issue; "experimentation needed to practice the invention must not be undue

experimentation." In re Wands, 858 F.2d 731, 737 (Fed. Cir. 1988) (*emphasis added*). Applicant asserts that the specification provides an ample number of examples disclosing actual experimentation guiding the skilled artisan to make and use the claimed invention without undue experimentation.

For example, the specification at Examples 2, 3 and 4 disclose the use of a cell line (OV1063) to generate a cDNA expression library likely to provide appropriate clonal representation of ovarian cancer antigens (Example 2). Subsequent screening of the expression library with serum obtained from a patient with serous ovarian carcinoma demonstrated strong reactivity with OV1063 cell lysates as well as with ovarian tumors (Example 3). Additional analysis of the polynucleotides contained within the OV1063 clones revealed that one clone expressed ABC-7 (ATP-binding iron transporter) polypeptides (Example 4).

Such actual experimentation reveals to one of skill in the art that assay systems may be developed which utilize the expression of ABC-7 polypeptides to screen suspect serum for the presence of auto-antibodies to ABC-7 polypeptides. The mechanics of detecting the presence of autoantibodies to ABC-7 and the other four peptides in the Markush-defined genus is within the abilities of one of skill in the art. Notwithstanding, the specification provides teachings of methods to detect the presence of autoantibodies bound to ABC-7 polypeptides, for example, through the use of alkaline phosphatase-conjugated anti-human IgG antibody to identify the presence of autoantibodies to ABC-7. Similar assays will detect autoantibodies bound to the other peptides disclosed in the specification.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of claim 41 under 35 U.S.C. § 112, 1st paragraph as allegedly containing subject matter in the specification which was not described in such a way as to enable one skilled in the art to which it pertains, or is most nearly connected, to make and/or use the invention.

Claim 41 was also rejected under 35 U.S.C. § 112, 1st paragraph as allegedly "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention." *See* Paper No. 15, page 7, lines 1-4. More specifically, the rejection states that "the claim encompasses a method comprising determining the presence of antibodies that bind any protein designated as such [ATP-dependent iron

transporter ABC-7], including isoforms or variants of the protein described by Allikmets et al which have not been described in the specification. Accordingly, the specification is insufficient to meet the written description requirements set forth under 35 U.S.C. § 112, 1st paragraph." *See* Paper No. 15, page 7, lines 11-15.

Applicant respectfully disagrees and traverses this rejection.

The office action appears to reject claim 41 as lacking written description for other proteins (e.g., variants) not disclosed or claimed by the invention. For example, the office action states that "the claims encompass a genus of variant species, [and that] an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice..." *See* Paper No. 15, page 8, lines 8-10.

Applicant asserts that the language of claim 41 is clear, as is the written description supporting this claim. Claim 41 claims a method of screening for cancer in an individual comprising obtaining a sample of bodily fluid from the individual and determining whether or not the sample contains antibodies specific for one or more of the proteins selected from the group consisting of ... ATP-dependent iron transporter ABC-7, the presence of antibodies supporting a diagnosis of cancer. Applicant has clearly identified "ABC-7" as Genbank sequence AF133659, and the claim scope encompasses antibodies that specifically bind this sequence, along with antibodies that bind the other four recited proteins. Applicant has discussed the presence of autoantibodies in cancer patients that are specific for a number of antigens that are normally intracellular. A polyclonal autoimmune response to one of these intracellular proteins can be detected by binding of antibodies to any variant of the specific protein. The presence of these autoantibodies can be correlated with neoplastic processes in patients, and therefore detection of autoantibodies can be used as a component of a cancer screening program. Therefore, Applicant has provided sufficient written description for the *claimed* invention.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of claim 41 under 35 U.S.C. § 112, 1st paragraph as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Rejections under 35 U.S.C. § 112, 2nd paragraph

Claims 85-89 were rejected under 35 U.S.C. § 112, 2nd paragraph, as allegedly "being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." More particularly, the rejection asserts that the use of the term "increased likelihood" in claim 41 yields a vague and indefinite claim. See Paper No. 15, page 9, lines 6-10.

Applicant respectfully disagrees and traverses this rejection.

According to the CCPA, "it is well established that 'claims are not to be read in a vacuum, and limitations therein are to be interpreted in light of the specification in giving them their 'broadest *reasonable* interpretation.'" In re Marosi, 710 F.2d 799, 802, 218 U.S.P.Q. (BNA) 289, 292 (CCPA 1983) (*quoting* In re Okuzawa, 537 F.2d 545, 548, 190 U.S.P.Q. (BNA) 464, 466 (CCPA 1976)).

"Definiteness problems often arise when words of degree are used in a claim. That some claim language may not be precise, however, does not automatically render a claim invalid." Seattle Box v Indus. Crating and Packing, 731 F.2d 818, 826, 221 USPQ 568, 573-574 (Fed. Cir. 1984). Regarding issues of definiteness of claim language, "the question becomes whether one of ordinary skill in the art would understand what is claimed when the claim is read in light of the specification." BJ Services v. Halliburton Energy Services, 2003 WL 21802236 (Fed. Cir. Aug. 06, 2003).

Applicant respectfully asserts that one of skill in the art readily understands what is meant by the use of the term "increased likelihood". This terminology encompasses words of degree, based on the presence or absence in a cancer patient of one or more autoantibodies to the proteins identified as ABC-7, HOXA7, HOXB7, Arf-1 and the protein encoded by the EcoRI/XhoI fragment of bacteriophage λ clone 44B.1. However, the mere use of terms of degree does not render a claim *per se* indefinite. The relevant question is whether one of skill in the art comprehends the scope of the claim(s) based on the language used when read in light of the specification. In the instant case, one of skill in the art would understand that the presence of one or more autoantibodies is a diagnostic aid that "increases" the probability or "likelihood" that a given patient is harboring a neoplastic cell population. The presence of one or more autoantibodies is but one factor useful in diagnosing the presence of a neoplastic cell population.

Accordingly, Applicant respectfully requests reconsideration and withdrawal of the rejection of claim 41 under 35 U.S.C. § 112, 2nd paragraph as allegedly indefinite in the use of the terminology "an increased likelihood."

Conclusion

Applicant believes that incorporation of the amendments and consideration of the above remarks has placed this application in a condition for allowance. Early notification of a favorable consideration is respectfully requested.

Respectfully submitted,

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Dated: September 15, 2003

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